

# Embracing uncertainty in health technology assessment

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## ***Valorisation***

Addenda

Health Technology Assessment (HTA) is a field aiming at informing decision makers about the value of health care technologies and has direct policy relevance as well as societal impact.<sup>1-3</sup> This emphasises that the analyses, tools, and method developed in the current thesis are not merely scientific exercises. The overall aim was to provide tools to improve the consideration of uncertainty during the assessments of health care technologies, likely leading to better-informed health policy decisions in the future. In this chapter, I discuss how the results of the current thesis have generated value and may continue to generate value in- and outside the scientific community. Value is defined in this context as “the process of creating value from knowledge, by making knowledge suitable and/or available for social (and/or economic) use and by making it suitable for translation into competing products, services, processes and new activities”.<sup>4</sup>

I will first describe the societal relevance of the current thesis for different stakeholders, and describe why and how the different products developed in the current thesis are innovative. This chapter is concluded with the steps that have been undertaken to disseminate the results of the current thesis.

## ***Societal relevance***

This section discusses the relevance of the results of this thesis for different stakeholder groups, namely health care professionals and patients, health policy decision makers, and HTA and health economics researchers.

First of all, the results of the current thesis have had a direct impact on care that can be provided by health care professionals to patients. The study describing the appraisal of fluocinolone acetonide implant (**Chapter 3**) is a summary of an actual appraisal which has resulted in the recommendation of fluocinolone acetonide intravitreal implant for the treatment of recurrent non-infectious uveitis in the United Kingdom. All documents that were produced during this appraisal are available online<sup>5</sup>, however, these documents are lengthy. By writing this publicly available summary, we hope to have provided a clear overview of the key uncertainties that arose during this appraisal and of the reasons why fluocinolone acetonide intravitreal implant was finally recommended. The subsequent chapters of this thesis also aim at impacting patients care by improving the consideration of uncertainty in health policy decisions. Systematically considering and assessing a broader range of uncertainty would result in better-informed health policy decisions, and facilitate (rapid) access to health care technologies providing value for money, and hopefully value to patients.

The second stakeholder group which benefits from the results of the current thesis are health policy decision makers. They directly benefited from our expertise, as an evidence review group, during the appraisal of fluocinolone acetonide intravitreal implant (**Chapter 3**). Additionally, **Chapter 2** argues that the implementation of registries and coverage with evidence development (CED) may benefit from a systematic identification of uncertainty before their implementation. This may improve the design of CED schemes by focusing on remaining uncertainties. The general discussion of this thesis further encourages the use of value of information (VOI) to inform CED research design and provides recommendations about how to improve the implementation of VOI and registries to inform health policy decisions. For instance, the set-up of mandatory protocols could contribute to improving the design of registries. The tools and method described in **Chapters 7 to 9** aim at improving the uncertainty identification and assessment in health economic evaluations and health policy decisions. The broader uptake of these tools and method in company submissions, or during the review of such submission may lead to more complete assessment of uncertainty than in current submissions.

Finally, HTA and health economics researchers benefit from the results of the current thesis. **Chapters 5 and 6** provide examples of how registry data can be used and analysed to assess the effectiveness and cost effectiveness of pharmaceuticals. Additionally, the tools and method developed in **Chapters 7 to 9** will be made freely available online for use once published. Using these tools systematically during model development may lead to more complete uncertainty assessment. Additionally, these tools encourage a more systematic reporting of which uncertainty is present and assessed during the assessment of health care technologies.

## ***Products and innovativeness***

**Chapters 6 to 9** resulted in innovative products described in this section. These product are partly already freely available online and the remainder will be made available online once published.

The health economic model developed in **Chapter 6** is freely available online.<sup>6</sup> This is innovative since health economic models are not routinely published online. We therefore contributed to open sciences by providing access to the source code, and consequently allow the re-use of (part of) the code for further assessments.

The ParamEtRic SURvivAl moDel sElection (PERSUADE) template (**Chapter 7**) is also freely available online (<https://github.com/Bram-R/PERSUADE>), and is the first

template aiming at standardising parametric survival model selection for health economic models.

The R code to estimate weights for multiple parametric survival models is described in **Chapter 8**. Survival model selection uncertainty is currently not routinely included when assessing the uncertainty surrounding health economic models. By providing this code, we hope to encourage health economic modellers to consider this uncertainty during their assessment.

Finally, **Chapter 9** describes the development of the TRansparent Uncertainty ASsessment (TRUST) tool, which is also freely available to anyone as an Appendix to the open source publication (<https://doi.org/10.1007/s40273-019-00855-9>).<sup>7</sup> To the best of my knowledge, no such tools promoting a transparent and systematic identification of uncertainty existed within the HTA literature.

## ***Dissemination***

The results of this thesis have been disseminated among the different stakeholder groups through different activities.

Almost all papers described in the current studies have been published open access in international scientific journals. This has permitted their dissemination among researchers but provides access to their content to all stakeholders if they desire to. Additionally, a short and non-technical article describing the advantage of treatment-line matching (**Chapters 5 and 6**) has been published in a non-peer reviewed journal (Value and Outcome Spotlight) published by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR). The complete report summarised in **Chapter 3** can also be freely accessed on the National Institute for Health and Clinical Excellence website.<sup>5</sup> Besides (open access) scientific publications, the products developed in **Chapters 6 to 9** will become available online once published.

Research performed as part of this thesis has also been presented at (inter)national conferences, which ensured their dissemination among the scientific community, employees of pharmaceutical and consultancy firms, as well as decision makers. The results of the current studies have been presented during ISPOR Europe, the European Health Economic Association (EuHEA) congress, the International Health Economic Association (iHEA congress), the Lowlands Health Economics Study Group, the Care and Public Health Research Institute (CAPHRI) Research Day, the 'Certainly uncertain' symposium of the Nederlands Vereniging voor Technologie Assessment in

de Gezondheidszorg (NVTAG), and the national symposium of the Vereniging voor Gezondheidseconomie (VGE).

To ensure the dissemination of TRUST among pharmacoeconomic assessors of the Dutch Health Care Institute (Zorginstituut Nederland) and thus during Dutch health policy decisions, TRUST has been applied during a prospective case study.<sup>8</sup> Additionally, TRUST has been used and presented during the appraisal of tomosynthesis as a screening instrument for the Dutch National Breast Cancer Screening Program. This ensured the dissemination of TRUST among decision makers. A workshop on uncertainty has also been held to present TRUST to a wide audience of stakeholders involved in the assessment and appraisal of health care technologies in the Netherlands and the United Kingdom (pharmacoeconomic assessors, decision makers, HTA researchers).

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